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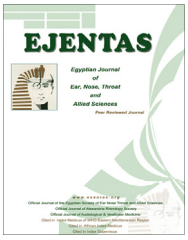

CASE REPORT

Kartagener's syndrome: A clinical reappraisal with two case reports

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Abstract Kartagener's syndrome is a rare congenital disorder consisting of sinusitis, bronchiectasis with situs inversus and is associated with infertility. It is the subgroup of disorder called primary ciliary dyskinesia in which well defined morphological or functional abnormalities of cilia result in sinopulmonary involvement with varying severity. Clinical manifestations involve chronic and/or recurrent respiratory infections with much heterogeneity in multisystem involvement. Early diagnosis and management of this condition help to prevent irreversible lung damage and prevent chronic lifelong sequelae.

1. Introduction

Primary ciliary dyskinesia, with an incidence of 1 in 20,000–30,000,[1] is an autosomal recessive condition characterised by bronchiectasis, sinusitis and otitis media. The coexistence of PCD and situs inversus is known as Kartagener's syndrome (KS) and it occurs in 50% of PCD cases.[2] It is because of an inherent defect in the ciliary ultrastructure, due to which ciliary motility and consequently its function are impaired. Mucociliary clearance, an intricate process by which cilia carry the mucous blanket of the upper respiratory tract to the gastrointestinal tract, is the basic mechanism by which the upper airway protects itself from exposure to pathogens, allergens, and toxins. In these cases there is an impaired mucociliary clearance, attributed to uncoordinated and inefficient ciliary movements, that predisposes to recurrent respiratory infections. In men, infertility is frequently seen because the structure of the sperm tail is identical to that of a motile cilium.[3] We hereby report two cases of this rare clinical entity with a clinical insight into it.

1.1. Case report 1

A 25 year old single female came to an ENT outpatient department with complaints of recurrent sneezing, rhinorrhoea, productive cough, on and off fever and breathlessness on exertion since childhood. Her previous records showed repeated hospital admissions for recurrent chest infections. She was allergic to dust. The expectoration was pale yellow, thick, mucoid and non-foul smelling. Nasal examination

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revealed boggy, bluish mucosa over bilateral inferior turbinates with mucoid nasal discharge. On chest auscultation there were crepitations and wheezes over bilateral lung fields. Routine blood investigations were normal except increased ESR (35 mm/Ist h). Sputum for acid fast bacilli was negative. Chest X-ray revealed dextrocardia with bronchiectatic changes seen in both lower lung fields (more on the left side) (Fig. 1). X-ray PNS showed opacity in frontal and maxillary sinuses bilaterally (Fig. 2). CT scan of thorax showed cystic and varicose bronchiectasis mainly in bilateral middle and lower lobes, peribronchial thickening and multiple tiny interstitial nodules. The organs of the chest and abdomen were abnormally positioned as mirror images of their normal arrangement (Figs. 3 and 4). A clinico-radiological diagnosis of Kartagener's syndrome was made and electrocardiogram also showed inverted P and T waves in lead I**,** negative deflection of QRS complex and poor progression of R wave in left side chest leads suggestive of dextrocardia**.** Conservative management was instituted and it comprised of inhaled steroid sprays, antibiotics, mucolytics and bronchodilators. She responded well to the treatment. She is in regular follow up.

1.2. Case report 2

A 26 year old single male came to us with complaints of left side nasal obstruction and watery rhinorrhea for the past 2 years. He also had a history of recurrent chest infections for which he received treatment several times at various places. There was no history of smoking or tuberculosis and he was born to non-consanguineous parents. Anterior rhinoscopy revealed a mild septal deviation to left with bilateral nasal polyposis with thick muco-purulent discharge. Diagnostic nasal endoscopy revealed polyps in bilateral middle meatus area and on middle turbinates. Routine blood counts were; Hb-17.2 g%, TLC- 15,000, DLC- N79 L18 E1 M2, ESR- 6 mm/Ist h. CT scan of paranasal sinuses showed bilateral diffuse sinonasal polyposis with increased attenuation and hyperdense

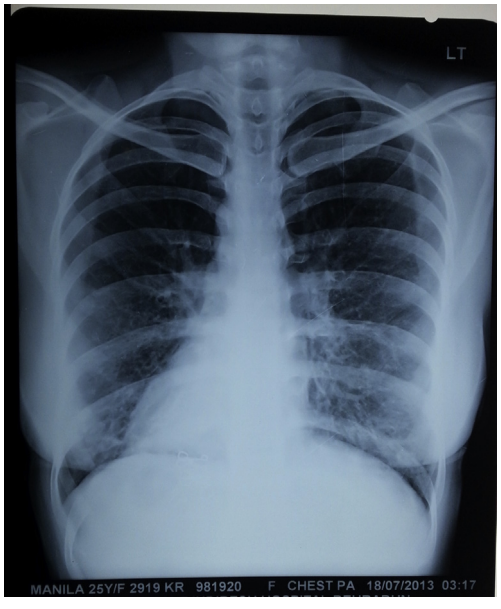

Figure 1 Chest X-ray showing dextrocardia with bronchiectatic changes in lower lung zones, more on the left side.

Figure 2 Sinus radiograph showing haziness in bilateral frontal and maxillary sinuses.

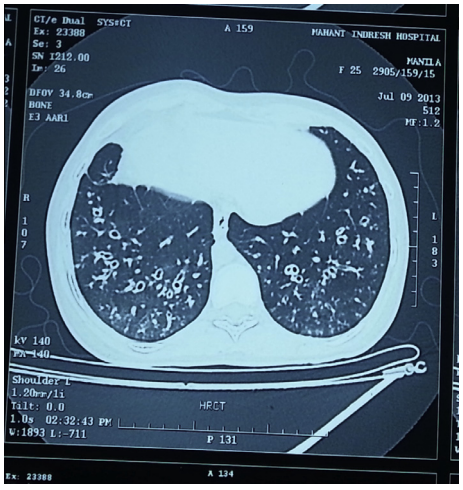

Figure 3 CT thorax shows bronchiectatic changes in both lower lung fields.

foci suggestive of inspissated secretions/fungal sinusitis (Fig. 5). Pre-operative investigations incidentally revealed dextrocardia and left lower zone bronchiectatic changes on chest radiography. ECG revealed changes consistent with dextrocardia. USG abdomen further confirmed situs inversus depicting the liver on the left side and the spleen on the right side. Colour Doppler study too revealed dextrocardia. A clinico-radiological diagnosis of Kartagener's syndrome was made. Family history revealed that his brother, too, was once diagnosed with right sided heart by a clinician on routine examination. He underwent functional endoscopic sinus surgery and removed polyps were sent to histopathology, which showed features of allergic fungal sinusitis. He is maintaining regular follow-up and is presently on steroid nasal spray and nasal douches. He is now relatively symptom free.

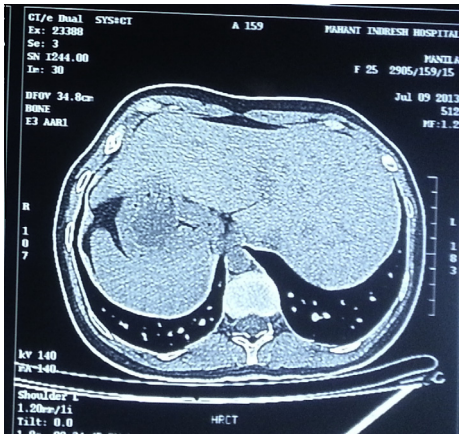

Figure 4 Abdominal cut (CT) shows situs inversus, the liver on the left side and the spleen and the stomach on the right side.

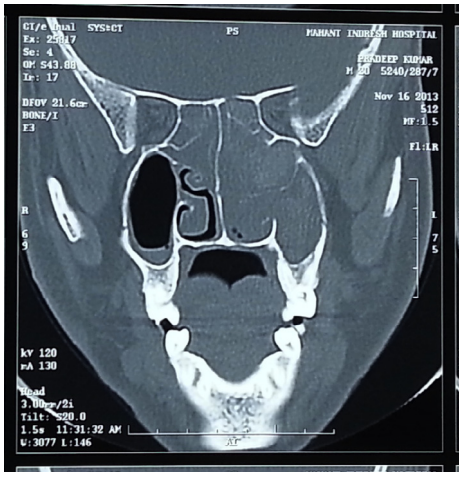

Figure 5 CT scan of paranasal sinuses showing bilateral diffuse sinonasal polyposis.

2. Discussion

The triple alliance of bronchiectasis, sinusitis and situs inversus was first cited by Stewart in 1904, but it was Swiss paediatrician Manes Kartagener, in 1933, who described it in detail and thus it bears his name thereafter. Pseudostratified ciliated columnar cells line the nasopharynx, middle ear, paranasal sinuses, larynx, trachea and bronchi. Any functional disruption of mucociliary clearance due to uncoordinated and ineffective ciliary movement can progress to connotation of long standing sinonasal, aural, and pulmonary problems. More than 200 proteins and polypeptides are involved in ciliary formation and structure,[4] most of which can be visualised clearly by electron microscopic examination. Ultrastructurally, a normal cilium consists of an axoneme and a pair of central singlet microtubules surrounded by nine pairs of doublets (the '9 + 2' pattern).[4] Other structures such as the bridge connecting central singlets, central sheath, radial spoke, outer and inner dynein arm, nexin link, and ciliary membrane are all crucial to maintain the normal integrity and function of the cilium. Any abnormality involving these structures may impair ciliary function. Most of the disease causing mutations are said to involve two genes coding for the dynein axonemal heavy chain 5 (DNA H5) and dynein axonemal intermediate chain 1 (DNAI1).[5]

The onset of clinical manifestations can be traced back to early childhood. There is usually a wide range of defects in ciliary ultrastructure and motility which impairs mucociliary clearance and thus causes sinopulmonary symptoms with varying severity. Nasal involvement occurs usually in the form of chronic rhinitis or sinusitis and nasal polyposis where nasal obstruction and rhinorrhea are the main complaints. Sinusitis in KS is the least distinctive feature and can coexist with the absence or hypoplasia of one or more sinuses, nasal polyposis or infection.[6] Ear problems can occur in the form of otitis media with effusion, and recurrent otitis media with or without a history of recurrent grommet insertion in childhood. Chronic productive cough and recurrent pulmonary infections are usual chest complaints. Haemoptysis may also be present. Dyspnoea or wheezing usually indicates either widespread bronchiectatic changes or underlying chronic obstructive pulmonary disease. Corneal abnormalities, headache and anosmia may also manifest in these patients.[7] Normal ciliary beating is also necessary for visceral rotation and orientation during embryonic development. Patients with KS may have either situs solitus i.e., dextrocardia only or situs inversus totalis where all the visceral structures are on opposite side.[8] Isolated dextrocardia is almost always associated with other serious cardiac and vascular anomalies**.** Delayed diagnosis culminates into progression of KS with complications such as bronchiectasis, pulmonary fibrosis, and finally impaired lung and/or heart function.[9]

The diagnosis of KS is often made incidentally on routine radiological examination. Chest X-ray is usually the first imaging modality that reveals dextrocardia and situs inversus as an incidental finding on routine checkup. Computed Tomography (CT) of thorax, further, may show malrotation or bronchiectatic changes and ultrasonogram of abdomen can also reveal situs inversus totalis. CT of paranasal sinuses delineates pansinusitis, polyposis or hypoplasia of sinuses. Screening tests like nasal saccharin transit time test',[10] which measures nasal mucociliary clearance, and nasal Nitric oxide measurements[11] are rapid and reliable screening methods which could be of immense help in making early diagnosis**.** Audiometry and tympanometry assist in detecting conductive hearing loss and presence of fluid in the middle ear. Spirometry studies help to assess the severity of pulmonary involvement. The cultures from lower respiratory tract most commonly yields *Haemophilus influenzae*, *Staphylococcus aureus*, *streptococcus pneumoniae* and rarely *Pseudomonas aeruginosa*.[12] Semen analysis for sperm motility and ultrastructure is helpful regarding fertility issues. Majority of infertile patients with KS have a normal sperm count, but with a structural defect and complete lack of motility.[13] Male patients with KS invariably are infertile, whereas females usually have reduced fertility.[13] Demonstration of abnormal ciliary movements by electron microscopic studies of biopsies taken from nasal mucosa or trachea remains the investigation of choice for making definitive diagnosis. However availability of this microscopic facility at specialised centres only, leaves the diagnosis to be made solely on clinical examination accompanied with imaging studies.

Treatment is intended to relieve symptoms and prevent irreversible complications. Treatment protocol includes medication, surgery, and some adjuvant therapies. Antibiotics are given for acute bacterial exacerbations and for prophylaxis, too, and availability and early institution of good antibiotics have invariably lessened the need of surgery in these patients. Inhaled corticosteroids, mucolytics, bronchodilators, influenza and pneumococcal immunisation and chest physiotherapy manoeuvers and positive expiratory pressure devices are recommended and are beneficial. Surgical treatment i.e., FESS is helpful in patients with nasal polyposis and chronic rhinosinusitis. Because the healing process is relatively slow due to ineffective mucociliary clearance, a regular and consistent postoperative follow up plays an important role to prevent recurrence and to reduce morbidities due to retained secretions, impaired mucociliary clearance, and susceptibility to chronic recurrent airway infections. Lobectomy and pneumonectomy are advised for localised lung damage with recurrent haemoptysis or respiratory exacerbations.[9] Infertile patients can be treated by advanced micromanipulation techniques that permit nonmotile or poorly motile sperm to penetrate, or by in vitro fertilisation techniques.[14] Genetic testing carries the immense future potential for developing gene therapy and so genetic counselling can play an important role in addressing social and psychological aspects of fertility issues among young couples and possibility of genetic risks in children.

3. Conclusion

Kartagener's syndrome may exhibit variable and atypical clinical presentations and severity due to its multisystem involvement and reverse positioning of internal organs. Although there is no specific treatment for this clinical entity, failure to diagnose this may subject the patient to unnecessary repeated admissions, investigations and inappropriate treatment.

Conflict of interest

We have no conflict of interest to declare.

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